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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,950	03/20/2002	Frederic J de Sauvage	P1748R1E	4737

7590 12/07/2005

Denise M. Kettelberger
P. O. Box 2903
Minneapolis, MN 55402-0903

EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,950	DE SAUVAGE ET AL.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-14,19,21,22 and 26-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18,20 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647. The Examiner for this Application is now Daniel C. Gamett.

2. The amendments of 08/22/2005 have been entered in full. Claims 1-34 are pending. Claims 1-14, 19, 21-22, and 26-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Claims 15-18, 20, and 23-25 are under consideration as they are drawn to methods of administering monoclonal antibodies for the treatment of asthma.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

4. All prior objections/rejections not specifically maintained in this office action are hereby withdrawn.

Objection

5. The disclosure is objected to because of the following informalities: The specification, on page 37, lines 10-16, discloses that the full-length native sequence TCCR gene described in FIG 3. (SEQ ID NO:1) and FIG. 4 (SEQ ID NO:2). Figures 3 and 4 and SEQ ID NO: 1 and SEQ ID NO:2 are amino acid sequences, not DNA sequences. SEQ ID NO: 3 and SEQ ID NO: 4 are DNA sequences. Correction is required.

Claim Rejections - 35 USC § 112

6. Claims 15-18, 20, and 23-25 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in the prior office action, claims 17, 18, and 20 were rejected as totally lacking enablement whereas for claims 15, 16, and 23-25, it was held that the specification provided enablement for administering anti-TCCR antibodies in order to prevent, inhibit or attenuate the differentiation of T-cells into Th2 cells, but does not enable any skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

7. Upon further consideration in view of Applicant's amendments, it evident that even the limited scope of enablement described in the prior office action is present in the instant specification only in the form of prophetic examples. In this case, enablement relies heavily on the state of the art. Given the knowledge that TCCR regulates T cell function, a person of skill in the art at the time of filing would reasonably be expected to be able to make a monoclonal, humanized, or single-chain antibody, although it is debatable whether the amount of experimentation required would be "undue". Antibodies are naturally bivalent, and therefore would crosslink TCCR molecules on the cell surface, which in turn would be expected to result in receptor activation. However, neither the specification nor the prior art provide sufficient guidance for a method of preventing or inhibiting the differentiation of T-

cells into the Th2 subtype, or for a method of treating allergic diseases, including asthma, comprising administration of a TCCR agonist antibody.

8. The specification fails to provide guidance for using agonist TCCR antibodies in a method of preventing or inhibiting differentiation of T-cells into the Th2 subtype, wherein the preventing or inhibiting occurs in a mammal. The only *in vivo* model in the specification discloses TCCR "knockout" Mice (see Example 2, pages 66-68, in particular) and further that TCCR -/- mice have a greater Th2 response (see Example 3, page 89, lines 6-7, in particular). In addition, the specification discloses that *in vitro* cultures of CD4+ cells from spleen and lymph nodes of TCCR deficient mice have a diminished Th1 response and an enhanced Th2 response (see Example 12, page 80, lines 17-20 and page 80, lines 33-page 81, line 8, in particular). These examples suggest that TCCR activity is needed for Th1 differentiation, but it does not follow that a TCCR agonist (antibody or other) would prevent or inhibit differentiation of T-cells into the Th2 subtype. A model for the effects of a TCCR agonist is IL27, the natural ligand for this receptor. Lucas *et al.*, (Proc Natl. Acad. Sci. U S A. 2003 Dec 9;100(25):15047-52) teach that IL27 has a Th1-like signaling profile, but that IL27 alone is not sufficient to induce the differentiation of naïve T cells (see Abstract). IL27 was found to suppress expression of GATA-3, a Th2-specific transcription factor, an effect that might be considered an attenuation of Th2 differentiation. Therefore, although prevention or inhibition of Th2 differentiation was a reasonable hypothesis for the action of a TCCR agonist at the time the instant application was filed, subsequent research has shown that this is not what a TCCR agonist would do. Therefore, the instant specification cannot be

enabling for a method of preventing or inhibiting the differentiation of T-cells into the Th2 subtype.

9. With regard to enablement of methods of disease treatment (claims 17, 18, and 20), Applicant argues in the remarks filed 08/22/2005, that Lewis (2002), Curr. Opin. Immun. 14: 644-651, supports the enablement of claim 17 because the claimed anti-TCCR agonist antibodies are not antigen-specific and therefore are analogous to anti-IgE antibodies, which are known to be efficacious. Applicant's argument has been fully considered, but it is not persuasive because the analogy between anti-TCCR agonist antibodies and anti-IgE antibodies is tenuous at best. IgE is a soluble factor, its biological activity is well known, and the goal of anti-IgE antibody therapy is to block its action. The proposed action the claimed invention is to activate TCCR, which is a newly described receptor on the cell surface.
10. Applicant further cites a Huang *et al.* reference in support of enablement of claim 17. The Huang *et al.* reference has not been made of record, and therefore, neither the evidence therein nor the arguments based on that evidence have been considered.
11. Therefore, rejections of claims 15-18, 20, and 23-25 are maintained in view of the above and for reasons of record.

Claim Rejections - 35 USC § 102

12. Claims 15-17, 23, and 25 remain rejected under 35 U.S.C. 102(a) as being anticipated by Mattson *et al.* (International Publication No. WO 99/40195; of record). Applicant's arguments filed 08/22/2005 have been fully considered but they are not persuasive. It is

noted that the claims do not limit TCCR to any particular sequence. Figure 5 of the instant specification shows human and mouse sequences that are highly divergent and yet both are "TCCR". The DCRS1 polypeptide taught by Mattson *et al.* is human TCCR, the single amino acid difference notwithstanding. The anti-DCRS1 agonist antibodies taught by Mattson *et al.* are therefore equivalent to the anti-TCCR of the instant specification and they inherently posses all of the same properties and effects.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

14. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

15. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 15-18, 20, and 23-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15-18, 20, and 23-25 of copending Application No. 10/663158 ('158). Although the conflicting claims are not identical, they are not patentably distinct from each other because, with the amendments of 08/22/2005, the instant claims now recite a species of method that would anticipate the

generic method of '158. Where instant claims 15 and 17 recite "an anti-TCCR agonist antibody", claims 15 and 17 of '158 recite "a TCCR polypeptide or agonist thereof". Otherwise, the limitations of the respective sets of claims are identical.

17. This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,792,850, issued August 11, 1998, to Baumgartner *et al.* It was noted in the prior office action that the Zcytor1 polypeptide disclosed in the '850 patent is 100% identical to the TCCR polypeptide sequence and that the '850 patent teaches administering agonist ligands for stimulating cell-mediated immunity and for stimulating lymphocyte proliferation. The '851 patent also teaches that bivalent antibodies may be agonists (column 17, lines 43-44). Therefore, the '851 patent anticipates the instant claims by teaching administration of the same antibodies to the same patient population. The administered antibodies would elicit every effect that they are inherently capable of producing, including stimulating lymphocyte proliferation and attenuating Th2 differentiation.

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D.,whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
1 December 2005

DAVID S. ROMEO
PRIMARY EXAMINER